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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/033,435	12/27/2001	David Botstein	P2930R1C5	9704

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 10/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/033,435	BOTSTEIN ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claim Objections

Claim 41 appears to have a typing error (undoubtedly due to the ferocity with which Word autocorrects), the copyright © symbol where the letter c is intended.

Claim Rejections - 35 USC § 112 – Second paragraph

1. Claims 35-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 35-37 are vague and indefinite because the phrase "comprising amino acids 1 or 22 to 125 of SEQ ID NO: 9" is open to two possible interpretations. The first interpretation is that the claim means,

An isolated polypeptide comprising amino acid 1 or amino acids 22 to 125 of SEQ ID NO: 9.

In this interpretation, the claim would therefore read on any polypeptide which comprises the first amino acid of SEQ ID NO: 9, which is a methionine or alternatively on any polypeptide which comprises amino acids 22-125 of SEQ ID NO: 9.

The second interpretation is that the claim means:

An isolated polypeptide comprising amino acids 1 to 125 of SEQ ID NO: 9 or amino acids 22 to 25 of SEQ ID NO: 9.

The prior art rejection over the claims assumes the first interpretation and that the claims encompass the single amino acid, methionine.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 35-37 and 41-46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of proteins which are different from the sequence of SEQ ID NO: 9 which is disclosed in the specification. The genus includes variants for which no written description is provided in the specification. This large genus is represented in the specification by only SEQ ID NO: 9. For claims 35-37, only a single amino acid, a methionine, is necessarily specificied. Thus, applicant has express possession of only one particular protein sequence in a genus, where even in

claims 41-43, where 95% homologous language will comprise hundreds of millions of different possibilities. Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains.

Not only are there no structural limitations or requirements which provide guidance on the identification of proteins related to SEQ ID NO: 9, but there are no functional limitations in the claim either. Thus, these claims fail on both prongs of the written description analysis since there is no function for the broad structures to define.

Further, these claims encompass alternately spliced versions of the proteins, allelic variants including insertions and mutations, inactive precursor proteins which have a removable amino terminal end, and only specific amino acid sequences have been provided. No written description of alleles, of upstream or downstream regions containing additional sequence, or of alternative splice variants has been provided in the specification.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will

> hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the protein by percent homology lacks any specific required structure. This is precisely the situation of naming a type of material which is generally known to likely exist, but, except for the specific SEQ ID NO: 9, is in the absence of knowledge of the material composition and fails to provide descriptive support for the generic claim to ".

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound solely but its functional utility, as a deletion, without any definition of the particular deletions claimed.

In the instant application, certain specific SEQ ID NOs are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any proteins other than SEQ ID NO: 9. Therefore, the

claims fail to meet the written description requirement by encompassing proteins which are not described in the specification.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 35-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Tang et al (J. Cell Biol. (1990) 110:617-624).

This rejection, as noted above, is based upon the interpretation of claims 35-37 in which a single methionine is the only element which the isolated polypeptide must comprise.

Tang teaches a protein, protein 4.1, which comprises a methionine (see abstract, "deletion of motif V in the untranslated region inserts a new initiator methionine"). With regard to claims 36 and 37, the methionine is fused to a 4.1 polypeptide, which is heterologous to the polypeptide of SEQ ID NO: 9, and which heterologous peptide is immunogenic (see page 618, column 2, subheading "preparation of antibodies against synthetic peptides"), therefore inherently requiring that the peptide can function as an epitope tag.

Allowable Subject Matter

6. Claims 38-40 are allowed.

7. The following is a statement of reasons for the indication of allowable subject matter: Claims 38-40 are drawn to proteins which comprise the full length sequence of SEQ ID NO: 9 (or are encoded by the deposited nucleic acid sequence). These claims do not permit alterations of the protein sequence and due to the mitogen activity shown in the specification, have a specific and substantial utility. Lastly, there is no art which teaches or suggests this particular full length protein sequence.

Response to Arguments

8. Applicant's arguments filed September 15, 2003 have been fully considered but they are not persuasive.

Applicant initially provides a discussion of the written description requirement.

Applicant then argues that claims 41-46 comply with the written description requirement because there is no substantial variation among the species. This is simply not correct. It is beyond well known in the art that a single amino acid change can significantly alter the function of a protein. The classic example of this phenomenon is the single amino acid change in human beta hemoglobin that causes sickle cell anemia. That single amino acid change of a valine for a glutamine renders the hemoglobin protein unable to properly function. Therefore, Applicant's legal argument is not scientifically based, since it is not correct to presume that there is insubstantial variation due to the 95% or hybridization language. In fact, the presumption is highly probable that random amino acid changes will significantly disrupt the protein. The current claims

permit a minimum of 5-6 amino acids to be altered within the protein and probably more for the hybridization claims which would be expected to significantly disrupt the function of the protein. Therefore, the scientific evidence leads to a legal conclusion that there is no insubstantial variation.

Applicant attempts to rely upon the written description training material, and example 14 in particular, to support the contention that 95% language is permitted. However, Applicant fails to appreciate a central difference between example 14 and the current situation. In example 14, the protein is an enzyme with specific catalytic properties. Enzymes are a well known class of proteins with known functional domains. This is in contrast to the current situation where the protein of SEQ ID NO: 9 is essentially entirely unknown. All that is known about this protein, other than the sequence, is the proteins ability to function in a particular assay. There is no reason to assume that the variation in functional elements would be insubstantial in this case, unlike in example 14, where enzymes are known to have conserved functional domains. Therefore, Example 14 does not apply. This is significantly more like Example 17, where the species are known to have related function, as in Applicant's claim, but where the structural relationship is unknown. In this context, the Federal Circuit in Lilly and more recent cases has found that the claims do not meet the written description requirement.

With regard to claims 44-46, the same argument applies. There is substantial variation among these species. Unlike in the domamine receptor case, where the example indicates that the protein is a member of a known class, dopamine receptors,

here the protein of SEQ ID NO: 9 is not a member of a known class. Therefore, here again, the analogy that Applicant attempts to make with Example 9 of the written description guidelines is not correct. There is no expectation or reason to think that a protein of unknown origin, without known domains and without known relationships, would be permissive of the significant and substantial variation that would result from the scope of claims 44-46. Unlike the dopamine receptor, a protein for whom a crystal structure prediction existed as early as 1991, the current protein has no information regarding domains or elements which are central to function and elements which are nonessential. Thus, Example 9 of the guidelines is not appropriate since the current protein does not fit the same factual pattern as that of the example.

For these reasons, the written description rejection is maintained.

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

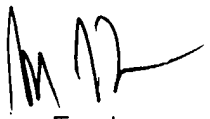
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is 703-308-6568. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Jeffrey Fredman
Primary Examiner
Art Unit 1634